

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Linda Burkly et al.

Application No.: Not Yet Assigned

Group Art Unit: Not Yet Assigned

Filed: September 8, 2003

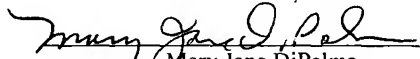
Examiner: Not Yet Assigned

For: METHODS OF MODULATING LIPID  
METABOLISM AND STORAGE

**CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. §1.8(a)**

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Date of Signature and of Mail Deposit

  
Mary Jane DiPalma

**INFORMATION DISCLOSURE STATEMENT (IDS)**

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Dear Sir:

Pursuant to 37 CFR 1.56, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached Form PTO-1449. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

Those patent(s) or publication(s) in the attached form Form PTO-1449 are not supplied because they were previously cited by or submitted to the Office in a prior application no. 09/704917, filed on November 2, 2000 and relied upon in this application for an earlier filing date under 35 U.S.C. 120.

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR 1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Commissioner is hereby authorized to charge any fees (with the exception of the filing fee) to our Deposit Account No. 18-1945, under Order No. CIBT-P02-115.

Respectfully Submitted,



David P. Halstead, Ph.D.  
Reg. No: 44,735

Date: September 8, 2003

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<b>Form PTO-1449</b> <b>INFORMATION DISCLOSURE</b> <b>CITATION</b> <b>IN AN APPLICATION</b> <i>(Use several sheets if necessary)</i>	Docket Number (Optional) CIBT-P02-115		Application Number	
	Applicant Burkly and Wang			
	Filing Date September 8, 2003		Group Art Unit	

**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	5,798,230	8/25/98	Bornkamm et al		
	AB	5,789,650	8/4/98	Lonberg et al.		
	AC	5,759,811	6/2/98	Epstein et al.		
	AD	5,747,641	5/5/98	Frankel et al.		
	AE	5,328,470	7/12/94	Nabel et al.		
	AF	5,223,409	6/29/93	Ladner et al.		
	AG	5,198,346	3/30/93	Ladner et al.		
	AH	5,122,464	6/16/92	Wilson et al.		
	AI	5,096,815	3/17/92	Ladner et al.		
	AJ	4,980,286	12/25/90	Morgan et al.		
	AK	4,874,702	10/17/89	Fiers et al.		
	AL	4,868,116	9/19/89	Morgan et al.		
	AM	4,588,585	5/13/86	Mark et al.		

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER		DATE	COUNTRY	CLASS	SUBCLA SS	Translation	
							YES	NO
	AN	WO 95/23223	8/31/95	PCT				
	AO	WO 95/18856	7/13/95	PCT				
	AP	WO 92/09690	6/11/92	PCT				
	AQ	WO 92/07573	5/14/92	PCT				
	AR	WO 91/06309	5/16/91	PCT				
	AS	WO 90/07861	7/26/90	PCT				
	AT	WO 89/07136	8/10/89	PCT				
	AU	WO 89/05345	6/15/89	PCT				
	AV	WO 89/02468	3/23/89	PCT				
	AW	WO 88/06630	9/7/88	PCT				
	AX	EP 412762	2/13/91	EPC				

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		<b>OTHER DOCUMENTS</b> <i>(Including Author, Title, Date, Pertinent Pages Etc.)</i>	
	AY	Agterberg et al., 1990, "Outer-membrane PhoE protein of Escherichia coli K-12 as an exposure vector: possibilities and limitations", Gene 88:37-45	
	AZ	Apelqvist et al., 1997, "Sonic hedgehog directs specialised mesoderm differentiation in the intestine and pancreas", Curr. Biol. 7:801-804	
	BA	Armentano et al., 1990, "Expression of human factor IX in rabbit hepatocytes by retrovirus-mediated gene transfer: potential for gene therapy of hemophilia B", Proc. Natl. Acad. Sci. USA 87:6141-6145	
	BB	Barbas et al., 1992, "Semisynthetic combinatorial antibody libraries: a chemical solution to the diversity problem", Proc. Natl. Acad. Sci. USA 89:4457-4461	
	BC	Berkner et al., 1988, "Development of adenovirus vectors for the expression of heterologous genes", Biotechniques 6:616-629	
	BD	Boerner et al., 1991, "Production of antigen-specific human monoclonal antibodies from in vitro-primed human splenocytes", J. Immunol. 147:86-95	
	BE	Breslow, 1996, "Mouse models of atherosclerosis", Science 272:685-688	
	BF	Callow et al., 1994, "Expression of human apolipoprotein B and assembly of lipoprotein(a) in transgenic mice", Proc. Natl. Acad. Sci. USA 91:2130-2134	
	BG	Chang et al., 1994, "Products, genetic linkage and limb patterning activity of a murine hedgehog gene", Development 120:3339-3353	
	BH	Charbit et al., 1986, "Probing the topology of a bacterial membrane protein by genetic insertion of a foreign epitope; expression at the cell surface", EMBO J. 5:3029-3037	
	BI	Chen et al., "Gene therapy for brain tumors: regression of experimental gliomas by adenovirus-mediated gene transfer in vivo", Proc. Natl. Acad. Sci. USA 91:3054-3057	
	BJ	Chowdhury et al. 1991, "Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR-deficient rabbits", Science 254:1802-1805	
	BK	Clackson et al., 1991, "Making antibody fragments using phage display libraries", Nature 352:624-628	
	BL	Co et al., 1991, "Humanized antibodies for antiviral therapy", Proc. Natl. Acad. Sci. USA 88:2869-2873	
	BM	Cull et al., 1992, "Screening for receptor ligands using large libraries of peptides linked to the C terminus of the lac repressor", Proc. Natl. Acad. Sci. USA 89:1865-1869	

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	BN	Cunningham and Wells, 1989, "High-resolution epitope mapping of hGH-receptor interactions by alanine-scanning mutagenesis", Science 244:1081-1085	
	BO	Cwirla et al., 1990, "Peptides on phage: a vast library of peptides for identifying ligands", Proc. Natl. Acad. Sci. USA 87:6378-6382	
	BP	Dai et al., 1992, "Gene therapy via primary myoblasts: long-term expression of factor IX protein following transplantation in vivo", Proc. Natl. Acad. Sci. USA 89:10892-10895	
	BQ	Dann et al., 1986, "Human renin: a new class of inhibitors", Biochem. Biophys. Res. Commun. 134:71-77	
	BR	Danos and Mulligan, 1988, "Safe and efficient generation of recombinant retroviruses with amphotropic and ecotropic host ranges", Proc. Natl. Acad. Sci. USA 85:6460-6464	
	BS	Devlin et al., 1990, "Random peptide libraries: a source of specific protein binding molecules", Science 249:404-406	
	BT	Echelard et al., 1993, "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity", Cell 75:1417-1430	
	BU	Eglitis et al., 1985, "Gene expression in mice after high efficiency retroviral-mediated gene transfer", Science 230:1395-1398	
	BV	Ekker et al., 1995, "Patterning activities of vertebrate hedgehog proteins in the developing eye and brain", Curr. Biol. 5:944-955	
	BW	Fan et al., 1995, "Long-range sclerotome induction by sonic hedgehog: direct role of the amino-terminal cleavage product and modulation by the cyclic AMP signaling pathway", Cell 81:457-654	
	BX	Fancy et al., 1996, "New chemistry for the study of multiprotein complexes: the six-histidine tag as a receptor for a protein crosslinking reagent", Chem. Biol. 3:551-559	
	BY	Farese et al, 1995, "Knockout of the mouse apolipoprotein B gene results in embryonic lethality in homozygotes and protection against diet-induced hypercholesterolemia in heterozygotes", Proc. Natl. Acad. Sci. USA 92:1774-1778	
	BZ	Ferry et al., 1991, "Retroviral-mediated gene transfer into hepatocytes in vivo", Proc. Natl. Acad. Sci. USA 88:8377-8381	
	CA	Flotte et al., 1993, "Expression of the cystic fibrosis transmembrane conductance regulator from a novel adeno-associated virus promoter", J. Biol. Chem. 268:3781-3790	

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	CB	Gordon et al., 1985, "Design of peptide derived amino alcohols as transition-state analog inhibitors of angiotensin converting enzyme", Biochem. Biophys. Res. Commun. 126:419-426	
	CC	Griffiths et al., 1993, "Human anti-self antibodies with high specificity from phage display libraries", EMBO J. 12:725-734	
	CD	Gross and Witkip, 1961, "Selective cleavage of the methionyl peptide bonds in ribonuclease with cyanogen bromide", J. Am. Chem. Soc. 83:1510	
	CE	Hall et al., 1995, "A potential catalytic site revealed by the 1.7-A crystal structure of the amino-terminal signalling domain of Sonic hedgehog", Nature 378:212-216	
	CF	Hansson et al., 1992, "Expression of recombinant proteins on the surface of the coagulase-negative bacterium Staphylococcus xylosus", J. Bacteriol. 174:4239-4245	
	CG	Hermonat et al., 1984, "Use of adeno-associated virus as a mammalian DNA cloning vector: transduction of neomycin resistance into mammalian tissue culture cells", Proc. Natl. Acad. Sci. USA 81:6466-6470	
	CH	Homanics et al., 1993, "Targeted modification of the apolipoprotein B gene results in hypobetalipoproteinemia and developmental abnormalities in mice", Proc. Natl. Acad. Sci. USA 90:2389-2393	
	CI	Huang and Stoller, 1991, "Construction of representative immunoglobulin variable region cDNA libraries from human peripheral blood lymphocytes without in vitro stimulation", J. Immunol. Methods 141:227-236	
	CJ	Huber et al., 1991, "Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: an innovative approach for cancer therapy", Proc. Natl. Acad. Sci. USA 88:8039-8043	
	CK	Hwu et al., 1993, "Functional and molecular characterization of tumor-infiltrating lymphocytes transduced with tumor necrosis factor-alpha cDNA for the gene therapy of cancer in humans", J. Immunol. 150:4104-4115	
	CL	Ike et al., 1983, "Solid phase synthesis of polynucleotides. VIII. Synthesis of mixed oligodeoxyribonucleotides by the phosphotriester solid phase method", Nucleic Acids Res. 11:477-488	
	CM	Itakura et al., 1981, Recombinant DNA, Proc. 3 <sup>rd</sup> Cleveland Symposium On Macromolecules, A.G. Walton, ed. (Elsevier, Amsterdam) pp. 273-289	
	CN	Itakura et al., 1984, "Expression in Escherichia coli of a chemically synthesized gene for the hormone somatostatin", Science 198:1056-1063	
	CO	Itakura et al., 1984, "Synthesis and use of synthetic oligonucleotides", Annu. Rev. Biochem. 53:323-356	

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	CP	Jones et al., 1986, "Replacing the complementarity-determining regions in a human antibody with those from a mouse", Nature 321:522-525	
	CQ	Kaufman and Sharp, 1982, "Construction of a modular dihydrofolate reductase cDNA gene: analysis of signals utilized for efficient expression", Mol. Cell. Biol. 2:1304-1319	
	CR	Kay et al., 1992, "Hepatic gene therapy: persistent expression of human alpha 1-antitrypsin in mice after direct gene delivery in vivo", Hum. Gene Ther. 3:641-647	
	CS	Kinto et al., 1997, "Fibroblasts expressing Sonic hedgehog induce osteoblast differentiation and ectopic bone formation", FEBS Lett. 404:319-323	
	CT	Klauser et al., 1990, "Extracellular transport of cholera toxin B subunit using Neisseria IgA protease beta-domain: conformation-dependent outer membrane translocation", EMBO J. 9:1991-1999	
	CU	Kohler et al., 1975, "Continuous cultures of fused cells secreting antibody of predefined specificity", Nature 256:495-497	
	CV	Kuwayama et al., 1988, "Presentation of an antigenic determinant from hen egg-white lysozyme on the flagellar filament of Escherichia coli", Bio/Tech. 6:1080-1083	
	CW	Leung et al., 1989, "A method for random mutagenesis of a defined DNA segment using a modified polymerase chain reaction", Technique 1:11-15	
	CX	Lindley, 1956, "A new synthetic substrate for trypsin and its application to the determination of the amino-acid sequence of proteins", Nature 178:647	
	CY	Linton et al., 1993, "Familial hypobetalipoproteinemia", J. Lipid Res. 34:521-541	
	CZ	Litngtung et al., 1998, "Sonic hedgehog is essential to foregut development", Nat. Genet. 20:58-61	
	DA	Mark et al, 1984, "Site-specific mutagenesis of the human fibroblast interferon gene", Proc. Natl. Acad. Sci. USA 81:5662-5666	
	DB	Marks et al., 1992, "Molecular evolution of proteins on filamentous phage. Mimicking the strategy of the immune system", J. Biol. Chem. 267:16007-16010	
	DC	McCormick et al., 1996, "Transgenic mice that overexpress mouse apolipoprotein B. Evidence that the DNA sequences controlling intestinal expression of the apolipoprotein B gene are distant from the structural gene", J. Biol Chem. 271:11963-11970	
	DD	Merrifield, 1967, "New approaches to the chemical synthesis of peptides", Recent Prog. Horm. Res23:451-482	

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	DE	Miller, 1990, "Progress toward human gene therapy", Blood 76:271-278	
	DF	Mohler and Vani, 1992, "Molecular organization and embryonic expression of the hedgehog gene involved in cell-cell communication in segmental patterning of Drosophila", Development 115:957-971	
	DG	Muzyczka et al., 1992, "Use of adeno-associated virus as a general transduction vector for mammalian cells", Curr. Top. Microbiol. Immunol. 158:97-129	
	DH	Myers et al., 1985, "A general method for saturation mutagenesis of cloned DNA fragments", Science 229:242-247	
	DI	Narang, 1983, "DNA synthesis", Tetrahedron 39:3-22	
	DJ	Needleman et al., 1970, "A general method applicable to the search for similarities in the amino acid sequence of two proteins", J. Mol. Biol. 48:443-453	
	DK	Orlandi et al., 1989, "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction", Proc. Natl. Acad. Sci. USA 86:3833-3837	
	DL	Persson et al., 1991, "Generation of diverse high-affinity human monoclonal antibodies by repertoire cloning", Proc. Natl. Acad. Sci. USA 88:2432-2436	
	DM	Powell-Braxton et al., 1998, "A mouse model of human familial hypercholesterolemia: markedly elevated low density lipoprotein cholesterol levels and severe atherosclerosis on a low-fat chow diet", Nat. Med. 4:934-938	
	DN	Purcell-Huynh et al., 1995, "Transgenic mice expressing high levels of human apolipoprotein B develop severe atherosclerotic lesions in response to a high-fat diet", J. Clin. Invest. 9:2246-2257 PMID: 7738190	
	DO	Queen et al., 1989, "A humanized antibody that binds to the interleukin 2 receptor", Proc. Natl. Acad. Sci. USA 86:10029-10033	
	DP	Riechmann et al., 1988, "Reshaping human antibodies for therapy", Nature 332:323-327	
	DQ	Roberts et al., 1992, "Directed evolution of a protein: selection of potent neutrophil elastase inhibitors displayed on M13 fusion phage", Proc. Natl. Acad. Sci. USA 89:2429-2433	
	DR	Rosenfeld et al., 1991, "Adenovirus-mediated transfer of a recombinant alpha 1-antitrypsin gene to the lung epithelium in vivo", Science 252:431-434	
	DS	Rosenfeld et al., 1992, "In vivo transfer of the human cystic fibrosis transmembrane conductance regulator gene to the airway epithelium", Cell 68:143-155	

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	DT	Sato et al., 1986, "Synthesis and antibiotic activity of a gramicidin s analogue containing bicyclic beta-turn dipeptides", J. Chem. Soc. Perkin Trans. 1:1231	
	DU	Schorr et al., 1991, "Surface expression of malarial antigens in Salmonella typhimurium: induction of serum antibody response upon oral vaccination of mice", Vaccine 9:675-681	
	DV	Scott et al., 1990, "Searching for peptide ligands with an epitope library", Science 249:386-390	
	DW	Scully et al., 1992, Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 35-1992. An eight-month-old boy with diarrhea and failure to thrive. N. Engl. J. Med. 327:628-635	
	DX	Taylor and Jones, 1979, "Multiple new phenotypes induced in 10T1/2 and 3T3 cells treated with 5-azacytidine", Cell 17:771-779	
	DY	Tempest, 1991, "Reshaping a human monoclonal antibody to inhibit human respiratory syncytial virus infection in vivo", Biotechnology (N Y) 9:266-271	
	DZ	Thiry et al., 1989, "Cloning of DNA sequences encoding foreign peptides and their expression in the K88 pili", Appl. Environ. Microbiol. 55:984-993	
	EA	Tratschin et al., 1984, "A human parvovirus, adeno-associated virus, as a eucaryotic vector: transient expression and encapsidation of the procaryotic gene for chloramphenicol acetyltransferase", Mol. Cell. Biol. 4:2072-2081	
	EB	Van Beusechem et al., 1992, "Long-term expression of human adenosine deaminase in rhesus monkeys transplanted with retrovirus-infected bone-marrow cells", Proc. Natl. Acad. Sci. USA 89:7640-7644	
	EC	Verhoeyen et al., 1988, "Reshaping human antibodies: grafting an antilysozyme activity", Science 239:1534-1536	
	ED	Wang et al., 1993, "Bone morphogenetic protein-2 causes commitment and differentiation in C3H10T1/2 and 3T3 cells", Growth Factors 9:57-71.	
	EE	Wells et al., 1985, "Cassette mutagenesis: an efficient method for generation of multiple mutations at defined sites", Gene 34:315-323	
	EF	Wilson et al., 1988, "Retrovirus-mediated transduction of adult hepatocytes", Proc. Natl. Acad. Sci. USA 85:3014-3018	
	EG	Wondisford et al., 1988, "Cloning of the human thyrotropin beta-subunit gene and transient expression of biologically active human thyrotropin after gene transfection", Mol. Endocrinol. 2:32-9	
	EH	Yang et al., 1997, "Expression of human GLI in mice results in failure to thrive, early death, and patchy Hirschsprung-like gastrointestinal dilatation", Mol. Med. 3:826-835	

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	EI	Young et al, 1995, "A genetic model for absent chylomicron formation: mice producing apolipoprotein B in the liver, but not in the intestine", J. Clin. Invest 96:2932-2946	
	EJ	Incardona et al., "The Teratogenic Veratrum Alkaloid Cyclopamine Inhibits Sonic Hedgehog Signal Transduction," Development 125:3553-3562 (1998)	
	EK	Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310 (1990)	
	EL	Chiang et al., "Cyclopia and Defective Axial Patterning in Mice Lacking Sonic Hedgehog Gene Function," Nature 383:407-413 (1996)	
EXAMINER			DATE CONSIDERED
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